

General

Guideline Title

Guidelines for the determination of brain death in infants and children: an update of the 1987 Task Force recommendations.

Bibliographic Source(s)

Nakagawa TA, Ashwal S, Mathur M, Mysore MR, Bruce D, Conway EE Jr, Duthie SE, Hamrick S, Harrison R, Kline AM, Lebovitz DJ, Madden MA, Montgomery VL, Perlman JM, Rollins N, Shemie SD, Vohra A, Williams-Phillips JA, Society of Critical Care Medicine, Section on Critical Care and Section on Neurology of the American Academy of Pediatrics, Child Neurology Society. Guidelines for the determination of brain death in infants and children: an update of the 1987 Task Force recommendations. Crit Care Med. 2011 Sep;39(9):2139-55. [91 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Report of Special Task Force. Guidelines for determination of brain death in children. American Academy of Pediatrics Task Force on Brain Death in Children. Pediatrics 1987;80:298–300.

Recommendations

Major Recommendations

The classification of the evidence (high, moderate, low, very low) and the strength of the recommendations (strong, weak, no specific recommendations) are defined at the end of the "Major Recommendations" field.

Summary Recommendations for the Diagnosis of Brain Death in Neonates, Infants, and Children

Recommendation	Evidence Score	Recommendation Score
 Determination of brain death in neonates, infants, and children relies on a clinical diagnosis that is based on the absence of neurologic function with a known irreversible cause of coma. Coma and apnea must coexist to diagnose brain death. This diagnosis should be made by physicians who have evaluated the history and completed the neurologic examinations. 	High	Strong

Re2onPrerequisites for initiating a brain death evaluation:	Evidence	Recommendation
	Signe	Saving
a. Hypotension, hypothermia, and metabolic disturbances that could affect the neurologic examination must be corrected before examination for brain death.		
b. Sedatives, analgesics, neuromuscular blockers, and anticonvulsant agents should be discontinued for a reasonable time period based on elimination half-life of the pharmacologic agent to ensure they do not affect the neurologic examination. Knowledge of the total amount of each agent (mg/kg) administered since hospital admission may provide useful information concerning the risk of continued medication effects. Blood or plasma levels to confirm high or supratherapeutic levels of anticonvulsants with sedative effects that are not present should be obtained (if available) and repeated as needed or until the levels are in the low to midtherapeutic range.	Moderate	Strong
c. The diagnosis of brain death based on neurologic examination alone should not be made if supratherapeutic or high therapeutic levels of sedative agents are present. When levels are in the low or in the midtherapeutic range, medication effects sufficient to affect the results of the neurologic examination are unlikely. If uncertainty remains, an ancillary study should be performed.	Moderate	Strong
d. Assessment of neurologic function may be unreliable immediately after cardiopulmonary resuscitation or other severe acute brain injuries and evaluation for brain death should be deferred for ≥24–48 hrs if there are concerns or inconsistencies in the examination.	Moderate	Strong
3. Number of examinations, examiners, and observation periods:		
a. Two examinations including apnea testing with each examination separated by an observation period are required.	Moderate	Strong
b. The examinations should be performed by different attending physicians involved in the care of the child. The apnea test may be performed by the same physician, preferably the attending physician who is managing ventilator care of the child.	Low	Strong
 c. Recommended observation periods: 1. Twenty-four hrs for neonates (37 wks gestation to term infants 30 days of age) 2. Twelve hrs for infants and children (>30 days to 18 yrs) 	Moderate	Strong
d. The first examination determines the child has met neurologic examination criteria for brain death. The second examination, performed by a different attending physician, confirms that the child has fulfilled criteria for brain death.	Moderate	Strong
e. Assessment of neurologic function may be unreliable immediately after cardiopulmonary resuscitation or other severe acute brain injuries and evaluation for brain death should be referred for ≥24–48 hrs if there are concerns or inconsistencies in the examination.	Moderate	Strong

commendation 4. Apriea testing:	Evidence Score	Recommendation Score
a. Apnea testing must be performed safely and requires documentation of an arterial $Paco_2$ 20 mm Hg above the baseline $Paco_2$ and ≥ 60 mm Hg with no respiratory effort during the testing period to support the diagnosis of brain death. Some infants and children with chronic respiratory disease or insufficiency may only be responsive to supranormal $Paco_2$ levels. In this instance, the $Paco_2$ level should increase to ≥ 20 mm Hg above the baseline $Paco_2$ level.	Moderate	Strong
b. If the apnea test cannot be performed as a result of a medical contraindication or cannot be completed because of hemodynamic instability, desaturation to <85%, or an inability to reach a Paco₂ of ≥60 mm Hg, an ancillary study should be performed.	Moderate	Strong
5. Ancillary studies:	'	
 a. Ancillary studies (electroencephalography and radionuclide cerebral blood flow) are not required to establish brain death unless the clinical examination or apnea test cannot be completed. 	Moderate	Strong
b. Ancillary studies are not a substitute for the neurologic examination.	Moderate	Strong
c. For all age groups, ancillary studies can be used to assist the clinician in making the diagnosis of brain death to reduce the observation period or when 1) components of the examination or apnea testing cannot be completed safely as a result of the underlying medical condition of the patient; 2) if there is uncertainty about the results of the neurologic examination; or 3) if a medication effect may interfere with evaluation of the patient. If the ancillary study supports the diagnosis, the second examination and apnea testing can then be performed. When an ancillary study is used to reduce the observation period, all aspects of the examination and apnea testing should be completed and documented.	Moderate	Strong
 d. When an ancillary study is used because there are inherent examination limitations (i.e., 1–3 in 5c), then components of the examination done initially should be completed and documented. 	High	Strong
e. If the ancillary study is equivocal or if there is concern about the validity of the ancillary study, the patient cannot be pronounced dead. The patient should continue to be observed until brain death can be declared on clinical examination criteria and apnea testing or a follow-up ancillary study can be performed to assist with the determination of brain death. A waiting period of 24 hrs is recommended before further clinical reevaluation or repeat ancillary study is performed. Supportive patient care should continue during this time period.	Moderate	Strong
6. Declaration of death:		

Recommendation	High Evidence	Strong Recommendation
	Score	Score
b. When ancillary studies are used, documentation of components from the second clinical examination that can be completed must remain consistent with brain death. All aspects of the clinical examination, including the apnea test, or ancillary studies must be appropriately documented.	High	Strong
c. The clinical examination should be carried out by experienced clinicians who are familiar with infants and children and have specific training in neurocritical care.	High	Strong

Abbreviations: $Paco_2 = partial pressure of arterial carbon dioxide.$

Note: The "evidence score" is based on the strength of the evidence available at the time of publication. The "recommendation score" is the strength of the recommendations based on available evidence at the time of publication. Scoring guidelines are listed in "Definitions" below.

Neurologic Examination Components to Assess for Brain Death in Neonates, Infants, and Children^a Including Apnea Testing

Reversible conditions or conditions that can interfere with the neurologic examination must be excluded before brain death testing. (See text in the original guideline document for discussion.)

Coma. The patient must exhibit complete loss of consciousness, vocalization, and volitional activity.
 Patients must lack all evidence of responsiveness. Eye opening or eye movement to noxious stimuli is absent.

Noxious stimuli should not produce a motor response other than spinally mediated reflexes. The clinical differentiation of spinal responses from retained motor responses associated with brain activity requires expertise.

Loss of all brain stem reflexes, including: Midposition or fully dilated pupils which do not respond to light.

Absence of pupillary response to a bright light is documented in both eyes. Usually the pupils are fixed in a midsize or dilated position (4–9 mm). When uncertainty exists, a magnifying glass should be used.

Absence of movement of bulbar musculature including facial and oropharyngeal muscles.

Deep pressure on the condyles at the level of the temporomandibular joints and deep pressure at the supraorbital ridge should produce no grimacing or facial muscle movement.

Absent gag, cough, sucking, and rooting reflex.

The pharyngeal or gag reflex is tested after stimulation of the posterior pharynx with a tongue blade or suction device. The tracheal reflex is most reliably tested by examining the cough response to tracheal suctioning. The catheter should be inserted into the trachea and advanced to the level of the carina followed by one or two suctioning passes.

Absent corneal reflexes.

Absent corneal reflex is demonstrated by touching the cornea with a piece of tissue paper, a cotton swab, or squirts of water. No eyelid movement should be seen. Care should be taken not to damage the cornea during testing.

Absent oculovestibular reflexes.

The oculovestibular reflex is tested by irrigating each ear with ice water (caloric testing) after the patency of the external auditory canal is confirmed. The head is elevated to 30°. Each external auditory canal is irrigated (one ear at a time) with approximately 10–50 mL of ice water. Movement of the eyes should be absent during 1 min of observation. Both sides are tested with an interval of several minutes.

3. Apnea. The patient must have the complete absence of documented respiratory effort (if feasible) by formal apnea testing demonstrating a $Paco_2 \ge 60 \text{ mm}$ Hg and $\ge 20 \text{ mm}$ Hg increase above baseline.

Normalization of the pH and Paco₂ measured by arterial blood gas analysis, maintenance of core temperature >35°C, normalization of blood pressure appropriate for the age of the child, and correcting for factors that could affect respiratory effort are a prerequisite to testing.

The patient should be preoxygenated using 100% oxygen for 5–10 mins before initiating this test.

Intermittent mandatory mechanical ventilation should be discontinued once the patient is well oxygenated and a normal Paco₂ has been achieved.

The patient's heart rate, blood pressure, and oxygen saturation should be continuously monitored while observing for spontaneous respiratory effort throughout the entire procedure.

Follow-up blood gases should be obtained to monitor the rise in Paco₂ while the patient remains disconnected from mechanical ventilation.

If no respiratory effort is observed from the initiation of the apnea test to the time the measured $Paco_2 \ge 60 \text{ mm Hg}$ and $\ge 20 \text{ mm Hg}$ above the baseline level, the apnea test is consistent with brain death.

The patient should be placed back on mechanical ventilator support and medical management should continue until the second neurologic examination and apnea test confirming brain death is completed.

If oxygen saturations fall 85%, hemodynamic instability limits completion of apnea testing, or a Paco₂ level of≥60 mm Hg cannot be achieved, the infant or child should be placed back on ventilator support with appropriate treatment to restore normal oxygen saturations, normocarbia, and hemodynamic parameters. Another attempt to test for apnea may be performed at a later time or an ancillary study may be pursued to assist with determination of brain death.

Evidence of any respiratory effort is inconsistent with brain death and the apnea test should be terminated.

4. Flaccid tone and absence of spontaneous or induced movements, excluding spinal cord vents such as reflex withdrawal or spinal myoclonus.

The patient's extremities should be examined to evaluate tone by passive range of motion assuming that there are no limitations to performing such an examination (e.g., previous trauma, etc.) and the patient observed for any spontaneous or induced movements.

If abnormal movements are present, clinical assessment to determine whether these are spinal cord reflexes should be done.

^aCriteria adapted from 2010 American Academy of Neurology criteria for brain death determination in adults.

Definitions:

Classification of Evidence

Grade	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

The strength of a recommendation reflects the extent to which the developers can be confident that desirable effects of an intervention outweigh undesirable effects.

Grade	Description
Strong	When the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not.
	 a. For patients—most people in your situation would want the recommended course of action and only a small proportion would not
	b. For clinicians—most patients should receive the recommended course of action
	c. For policymakers—the recommendation can be adopted as a policy in most situations
Weak	Evidence suggests that desirable and undesirable effects are closely balanced or the quality of evidence is low.
	 a. For patients—most people in your situation would want the recommended course of action but many would not b. For clinicians—you should recognize that different choices will be appropriate for different patients and you must help each patient to arrive at a management decision consistent with his or her values and preferences c. For policymakers—policymaking will require substantial debate and involvement of many stakeholders
No specific recommendations	The advantages and disadvantages of the recommendations are equivalent or where there is insufficient evidence on which to formulate a recommendation.

Clinical Algorithm(s)

A clinical algorithm to diagnose brain death in infants and children is provided in Appendix 8 of the original guideline document.

Scope

Disease/Condition(s)

Brain death

Guideline Category

Evaluation

Clinical Specialty

Anesthesiology

Critical Care

Neurology

Nuclear Medicine

Pediatrics

Radiology

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Nurses

Guideline Objective(s)

- To review the neonatal and pediatric literature from 1987, including any prior relevant literature, and update recommendations regarding
 appropriate examination criteria and use of ancillary testing to diagnose brain death in neonates, infants, and children
- To develop a checklist to provide guidance and standardization to document brain death

Target Population

Neonates, infants, and children thought to be brain dead

Interventions and Practices Considered

- 1. Correction of conditions affecting evaluation of brain death (hypotension, hypothermia, metabolic disturbances)
- 2. Discontinuation of medications affecting the neurological examination (sedatives, neuromuscular blockers, anticonvulsants)
- 3. Timing of neurologic evaluation in relation to cardiopulmonary resuscitation or other severe acute brain injury
- 4. Number of neurological examinations
- 5. Number of examiners
- 6. Duration of observation
- 7. Apnea testing
- 8. Ancillary studies (electroencephalography, radionuclide cerebral blood flow)*
- 9. Declaration of death

Major Outcomes Considered

- Survival rate following removal of ventilator support
- Diagnostic yield of the initial electroencephalogram vs. radionuclide cerebral blood flow studies in brain-dead children

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

A MEDLINE search of relevant literature published from January 1987 to June 2008 was conducted. Key words included: brain death, neurologic death, neonatal, pediatric, cerebral blood flow, electroencephalography, apnea test, and irreversible coma with the subheading "children." Additional articles cited in the post-1987 literature that were published before 1987 were also reviewed if they contained data relevant to this guideline.

^{*}Ancillary studies are not a substitute for the neurologic examination.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Classification of Evidence

Grade	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Abstracts and articles were independently reviewed and summarized by at least two individuals on each committee. Data were summarized into five categories: clinical examination, apnea testing, observation periods, ancillary tests, and other considerations.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

A multidisciplinary committee composed of physicians and nurses with expertise in pediatrics, pediatric critical care, neonatology, pediatric neurology and neurosurgery, nuclear medicine, and neuroradiology was formed by the Society of Critical Care Medicine (SCCM) and the American Academy of Pediatrics to update the guidelines for the diagnosis of pediatric brain death. The committee was divided into three working groups, each charged with reviewing the literature on brain death in neonates, infants, and children for the following specific areas: 1) examination criteria and observation periods; 2) ancillary testing; and 3) declaration of death by medical personnel, including legal and ethical implications.

No randomized control trials examining different strategies regarding the diagnosis of brain death exist. Standard evidenced-based approaches for guidelines used by many organizations attempting to link the "strength of the evidence" to the "strength of the recommendations" therefore cannot be used in this instance. There is, however, considerable experiential consensus within observational studies in the pediatric population. Grading of Recommendations Assessment, Development and Evaluation (GRADE), a recently developed standardized methodologic consensus-based approach, allows panels to evaluate the evidence and opinions and make recommendations. GRADE uses five domains to judge the balance between the desirable and undesirable effect of an intervention. Strong recommendations are made when there is confidence that the desirable effects of adherence to a recommendation outweigh the undesirable effects. Weak recommendations indicate that the desirable effects of

adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident. No specific recommendations are made when the advantages and disadvantages of alternative courses of action are equivalent or where there is insufficient evidence on which to formulate a recommendation. See the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields.

Each committee member assigned a GRADE score for 1) the strength of evidence linked to a specific recommendation and 2) indicated a) "yes," b) "no," or c) "uncertain" for each of the six recommendations. By *a priori* consensus, the committee decided that a "strong" recommendation could only be made if >80% of the committee members voted "yes" for a recommendation and that a "weak" recommendation was made if >60% but <80% voted "yes." "No recommendation" was made if <60% of the committee voted "yes" for a specific recommendation.

Rating Scheme for the Strength of the Recommendations

Strength of the Recommendations

The strength of a recommendation reflects the extent to which the developers can be confident that desirable effects of an intervention outweigh undesirable effects.

Grade	Description
Strong	When the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not.
	 a. For patients—most people in your situation would want the recommended course of action and only a small proportion would not
	b. For clinicians—most patients should receive the recommended course of action
	c. For policymakers—the recommendation can be adopted as a policy in most situations
Weak	Evidence suggests that desirable and undesirable effects are closely balanced or the quality of evidence is low.
	 a. For patients—most people in your situation would want the recommended course of action but many would not b. For clinicians—you should recognize that different choices will be appropriate for different patients and you must help each patient to arrive at a management decision consistent with his or her values and preferences c. For policymakers—policymaking will require substantial debate and involvement of many stakeholders
No specific recommendations	The advantages and disadvantages of the recommendations are equivalent or where there is insufficient evidence on which to formulate a recommendation.

Cost Analysis

A formal cost analysis was not performed and published analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

This document has been reviewed and endorsed by the following societies: American Academy of Pediatrics (section on Critical Care and section on Neurology), American Association of Critical Care Nurses, Child Neurology Society, National Association of Pediatric Nurse Practitioners, Society of Critical Care Medicine, Society for Pediatric Anesthesia, Society of Pediatric Neuroradiology, and World Federation of Pediatric Intensive and Critical Care Societies. The American Academy of Neurology affirms the value of this manuscript. The American Academy of Pediatrics (various subsections) had the opportunity to review and comment on this document. The Pediatric Section of the American Association

of Neurosurgeons and the Congress of Neurologic Surgeons have also been provided the opportunity to review this document.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

No randomized control trials examining different strategies regarding the diagnosis of brain death exist.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate determination of brain death in neonates, infants, and children
- Standardization of the diagnostic criteria for determination of brain death
- Accurate and well-documented assessment of pediatric brain death

Potential Harms

Not stated

Contraindications

Contraindications

- Apnea testing may be contraindicated in patients with significant lung injury, hemodynamic instability, or high spinal cord injury.
- Contraindications to apnea testing may include conditions that invalidate the apnea test (such as high cervical spine injury) or raise safety
 concerns for the patient (high oxygen requirement or ventilator settings.

Qualifying Statements

Qualifying Statements

The committee recognizes that medical judgment of involved pediatric specialists will direct the appropriate course for the medical evaluation and diagnosis of brain death. The committee also recognizes that no national brain death law exists. State statutes and policy may restrict determination of brain death in certain circumstances. Physicians should become familiar with laws and policies in their respective institution. The committee also recognizes that variability exists for the age designation of pediatric trauma patients. In some states, the age of the pediatric trauma patient is defined as <14 yrs of age. Trauma and intensive care practitioners are encouraged to follow state/local regulations governing the specified age of pediatric trauma patients. The committee believes these guidelines to be an important step in protecting the health and safety of all infants and children. These revised guidelines and accompanying checklist are intended to provide a framework to promote standardization of the neurologic examination and use of ancillary studies based on the evidence available to the committee at the time of publication.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Chart Documentation/Checklists/Forms

Clinical Algorithm

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Nakagawa TA, Ashwal S, Mathur M, Mysore MR, Bruce D, Conway EE Jr, Duthie SE, Hanrick S, Harrison R, Kline AM, Lebovitz DJ, Madden MA, Montgomery VL, Perlman JM, Rollins N, Shemie SD, Vohra A, Williams-Phillips JA, Society of Critical Care Medicine, Section on Critical Care and Section on Neurology of the American Academy of Pediatrics, Child Neurology Society. Guidelines for the determination of brain death in infants and children: an update of the 1987 Task Force recommendations. Crit Care Med. 2011 Sep;39(9):2139-55. [91 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1987 (revised 2011)

Guideline Developer(s)

American Academy of Pediatrics - Medical Specialty Society

Child Neurology Society - Medical Specialty Society

Society of Critical Care Medicine - Professional Association

Source(s) of Funding

Society of Critical Care Medicine (SCCM)

Guideline Committee

Not stated

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

The authors have not disclosed any potential conflicts of interest.

Guideline Endorser(s)

American Association of Critical-Care Nurses - Professional Association

National Association of Pediatric Nurse Practitioners - Professional Association

Society for Pediatric Anesthesia - Medical Specialty Society

Society for Pediatric Neuroradiology - Medical Specialty Society

World Federation of Pediatric Intensive and Critical Care Societies - Nonprofit Organization

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Report of Special Task Force. Guidelines for determination of brain death in children. American Academy of Pediatrics Task Force on Brain Death in Children. Pediatrics 1987;80:298–300.

Guideline Availability

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Electronic copies: Available in Portable Document Format (PDF) from the Society of Critical Care Medicine (SCCM) Web site	
Print copies: Available from the Society of Critical Care Medicine, 500 Midway Drive, Mount Prospect, IL 60056; Phone: (847) 827-6886; on-line through the SCCM Bookstore.	27-6869; Fax:

Availability of Companion Documents

The appendices to the original guideline document contain a brain death examination checklist.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on December 16, 2011. The information was verified by the guideline developer on January 18, 2012.

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